

REMARKS

Reconsideration and withdrawal of the rejections of the application respectfully requested in view of the amendments, remarks and enclosures herewith, which place the application in condition for allowance.

I. Status Of Claims And Formal Matters

Claims 1 to 27 are pending in this application. Claims 22 to 27 have been canceled, as allegedly being drawn to a non-elected invention. Claims 2, 6, 7, 17 and 18 have been canceled, without prejudice. Claims 1, 3, 9, 12 and 20 have been amended without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents. Claims 28 to 35 have been added. No new matter has been added.

Claim 1 has been clarified by adding the subject matter of claims 2, 6 and 7. Claim 3 has been clarified to depend from a non-cancelled claim. Claims 9 and 20 have been clarified to define CAR. Support for the recitation of coxsackie adenovirus receptor is found on page 42, line 21 to page 43, line 1. Claim 12 has been clarified by adding the subject matter of claims 17 and 18. Claims 28 to 35 mirror the subject matter of claims 12 to 16 and 19 to 21. No new matter has been added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. The Objections To The Claims Are Overcome

Claims 9 and 20 were objected to because the term "CAR-independent" should allegedly be spelled out in full at the first occurrence of the term. In response, Applicants have clarified claims 9 and 20 to recite coxsackie adenovirus receptor, thereby rendering the objection moot.

Reconsideration and withdrawal of the objection to the claims is respectfully requested.

III. The Rejections Under 35 U.S.C. §112, First Paragraph, Are Overcome

Claims 1 to 21 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner alleges that the specification is enabling for:

- (a) A method of increasing the ability of an adenovirus to transduce a specific cell

type relative to an unmodified adenovirus, comprising the step of modifying a gene encoding an adenoviral capsid protein by introducing a DNA sequence encoding a small peptide into said gene or by introducing a DNA sequence encoding a single chain antibody into either the 5' end of the minor capsid pIIIa gene or the 3' end of the minor capsid protein pIX gene;

(b) A method of killing tumor cells in an individual, said method comprising the steps of: injecting directly to said tumor cells an effective amount of recombinant adenoviruses comprising a therapeutic gene that converts a non-toxic compound to a toxic compound and a gene encoding a pIIIa protein or a pIX protein modified by introducing a single chain antibody into the N-terminus of said pIIIa protein or the C-terminus of said pIX protein; and treating said individual with an effective amount of said non-toxic compound.

Although the Applicant does not agree with the Examiner, in the interest of expediting prosecution, claims 1 and 12 have been clarified to conform with the above-cited recitations, which according to the Examiner, is enabled by the specification. Accordingly, Applicant respectfully submits that the rejection has been obviated.

Reconsideration and withdrawal of the Section 112, First Paragraph, rejections are earnestly requested.

IV. The Rejections Under 35 U.S.C. §112, Second Paragraph, Are Overcome

Claims 1 to 11 were rejected under 35 U.S.C. § 112, second paragraph, because the term “increasing the ability of an adenovirus” in claim 1 and its dependent claims is a relative term which allegedly renders the claim indefinite.

In response, Applicant respectfully point out that claim 1 has been clarified to recite method of increasing the ability of an adenovirus to transduce a specific cell type relative to an unmodified adenovirus, thereby rendering the rejection moot.

Reconsideration and withdrawal of the Section 112, Second Paragraph, rejections are earnestly requested.

V. The Rejections Under 35 U.S.C. §102 Are Overcome

Claims 1, 6 to 9 and 11 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Romanczuk et al. (WO 99/36545) (hereinafter “Romanczuk”) as evidenced by Wickham et al. (U.S. Patent No. 5,962,311) (hereinafter “the Wickham patent”). Claims 1, 8, 9 and 11 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Wickham et al. (U.S. Patent No. 5,962,311). Claims 1, 8 and 9 are rejected under 35 U.S.C. § 102(b) as

allegedly being anticipated by Wickham et al. (J. Virol. 71:8221-8229, 1997) (hereinafter “the Wickham article”).

The instant invention is directed to, *inter alia*, a method of increasing the ability of an adenovirus to transduce a specific cell type relative to an unmodified adenovirus, comprising the step of: modifying a gene encoding an adenoviral capsid protein by introducing a DNA sequence encoding a single chain antibody into either the 5' end of the minor capsid protein pIIIa gene or the 3' end of the minor capsid protein pIX gene, wherein said modification increases the ability of said adenovirus to transduce a specific cell type relative to an unmodified adenovirus. The invention is also directed to a method of killing tumor cells in an individual, said method comprising the steps of: injecting directly to said tumor cells an effective amount of recombinant adenoviruses comprising a therapeutic gene that converts a non-toxic compound to a toxic compound and a gene encoding a gene encoding a pIIIa protein or a pIX protein modified by introducing a single chain antibody into the N-terminus of said pIIIa protein or the C-terminus of said pIX protein; and treating said individual with said non-toxic compound. Such methods are not disclosed, taught or suggested by Romanczuk, the Wickham patent or the Wickham article.

The cited documents do not anticipate the instant invention. Romanczuk relates to a recombinant adenovirus having encoded modified capsid proteins which comprise heterologous peptide ligands. A single chain antibody is not a peptide ligand. Romanczuk does not teach or suggest a capsid protein encoding a single chain antibody. The Wickham patent relates to a recombinant adenovirus containing a modified adenovirus fiber protein comprising a constrained non-native short sequence of amino acids. A single chain antibody is not a short sequence of amino acids. The Wickham patent does not teach or suggest a capsid protein encoding a single chain antibody. The Wickham article relates to Ad vectors that contain a high-affinity αv integrin binding motif or a polylysine, heparin binding motif. Neither of these motifs are single chain antibodies. The Wickham article does not teach or suggest a capsid protein encoding a single chain antibody. Accordingly, Romanczuk, the Wickham patent or the Wickham article do not teach or suggest, alone or in combination, the presently claimed subject matter.

Reconsideration and withdrawal of the Section 102 rejections are earnestly requested.

VI. The Double-Patenting Rejections Are Overcome

Claims 1 to 11 were provisionally rejected under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 17 to 27 of copending Application No. 10/424,409.

The issue of whether there is indeed double patenting is contingent upon whether the remarks herewith are indeed considered and entered; and, if so, whether the Examiner believes there is overlap with claims ultimately allowed in the application.

Accordingly, reconsideration and withdrawal of the double patenting rejection, or at least holding it in abeyance until agreement is reached as to allowable subject matter, is respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Office Action is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks and amendments the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
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